

Case report

Beçhet's disease presenting with mononeuritis multiplex

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Beçhet's disease was probably first described by Hippocrates,¹ "Many had their mouths affected with aphthous ulcerations. There were also many defluxations about the genital parts, boils externally and internally about the groins". In 1937, Hulusu Beçhet described the clinical triad of oral ulceration, genital ulceration and uveitis, now known to us by his name.² The presence of multiple mononeuropathies in a patient with Beçhet's disease is rare, and has not previously been reported outside Japan. We describe a patient with Beçhet's disease who presented with skin folliculitis and a rapidly progressive clinical picture of mononeuritis multiplex and died from brain stem involvement.

CASE REPORT

A 51-year-old construction worker was admitted to a district general hospital with weakness of the left hand and mild unsteadiness of gait. Four months earlier he had attended a skin clinic with a persistent rash on his lower legs: skin biopsy had shown folliculitis, but no evidence of vasculitis. The weakness in his left arm progressed, his gait deteriorated and he developed sore red eyes. When transferred to the neurological department he was thin and depressed. He was afebrile. There were a few small aphthous ulcers on his tongue, but no genital ulceration, and a pustular erythematous rash on both legs below the knees, with marked bilateral ankle oedema (Fig 1). Both conjunctivae were congested and the right pupil was dilated and reacted sluggishly to light. Visual acuity in the right eye was restricted to appreciation of hand movement only, but was normal in the left eye. Slit-lamp examination revealed the presence of cells, flare and keratic precipitates in keeping with bilateral anterior uveitis. Fundoscopy showed retinal vasculitis in the right eye. There was severe weakness of the left hand and of wrist extension, and moderate weakness of elbow extension. Power in the right arm was normal. There was severe weakness distally in both legs. Reflexes were normal in the arms, but diminished in the legs. Sensation was intact. He could walk with assistance. He required urinary catheterisation shortly after admission.

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The ESR was 120 mm/hr, C-reactive protein 22.5 mg/l (normal < 6 mg/l), aspartate transaminase 50 U/l (normal range 10–40 U/l), alanine transaminase 156 U/l (normal range 10–45 U/l), total haemolytic complement 763 units/ml (normal range 250–700 units/ml) and immune complexes 263 microgram/ml (normal range 0–49 microgram/ml). Motor nerve conduction was slow in the left upper limb. Sensory potentials were not recordable. Repeat skin biopsy showed changes consistent with folliculitis, with no evidence of vasculitis.

The neurological presentation was of mononeuritis multiplex, but the associated uveitis led us to consider Beçhet's disease, sarcoidosis or the acquired immune deficiency syndrome. The additional features of aphthous ulceration and folliculitis suggested that Beçhet's disease was the most likely diagnosis. In spite of treatment with prednisolone 80 mg daily and azathioprine 50 mg twice daily, he developed progressive distal weakness in the arms and legs, and his general condition deteriorated. Azathioprine therapy was discontinued after 10 days, due to thrombocytopenia.

Six weeks following admission he developed slurred speech, right-sided facial weakness and a gaze palsy to the right. CT scan of the head showed multiple low attenuation non-enhancing areas in the brain-stem and periventricular areas. CSF protein was 1.5 g/l, glucose 3.3 mmol/l (plasma glucose 6.8 mmol/l), and there were no white cells. Cyclophosphamide 50 mg tid was added to the steroid therapy, but his condition deteriorated with the development of bilateral bronchopneumonia and he died seven weeks after admission.

At autopsy, sections of the cerebral hemispheres and brain stem revealed multiple foci of perivascular lymphocytic cuffing with fibrinoid necrosis of the vessel walls, in keeping with vasculitis. Small areas of infarction were also seen, although the neurones were well preserved, and also areas of meningeal reaction with lymphocytic infiltration and of demyelination. The overall appearances were of an intense vasculitic inflammation and encephalitis, but the degree of inflammation was out of proportion to the vascular involvement.

Sections from the spinal cord showed prominent demyelination particularly in the posterior and lateral columns of the cord, and vasculitis with fibrinoid necrosis of the walls of the blood vessels. Sections from several peripheral nerves showed foci of lymphocytic infiltration within the nerve bundles (Fig 2), amounting to nerve infarction, and the perineural vessels also showed evidence of vasculitis. Sections from skeletal muscle showed mild variation in fibre size with evidence of fibre grouping, in keeping with denervation. There were also vasculitic lesions elsewhere including the liver, spleen and small nerve plexuses in the urinary bladder.



Fig 1. Rash on lower legs due to folliculitis.

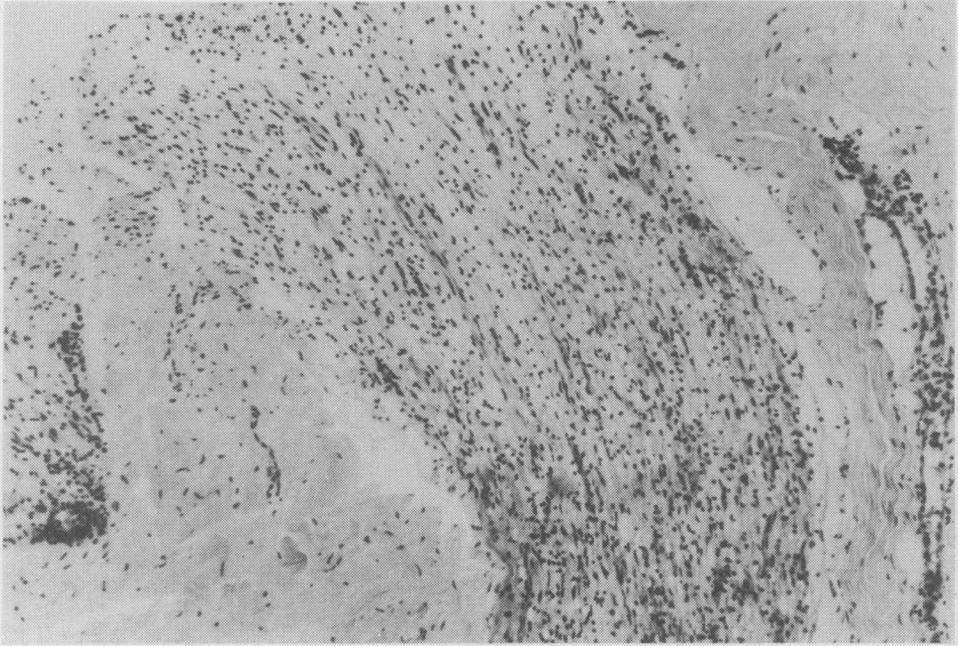


Fig 2. Peripheral nerve (H&E stain) × 60 magnification. Nerve infarct and vasculitis.

DISCUSSION

The clinical triad of relapsing iritis and ulcers of the mouth and genitalia named after Beçhet² is part of a systemic disorder of unknown aetiology. Other manifestations include erythema nodosum, folliculitis, pyoderma, thrombophlebitis, pericarditis, arthritis, epididymitis and ulcers of the gastrointestinal tract.³ The diagnosis of Beçhet's disease may be missed or delayed if only the classic triad is sought. In the absence of any single specific diagnostic test for Beçhet's disease, various sets of diagnostic criteria have evolved. Major features of the disease include orogenital ulceration, eye lesions and skin lesions.⁴ Minor features include central nervous system (especially brain stem) involvement, arthralgia or arthritis, intestinal ulcers and epididymitis. A definite diagnosis can be made if three major features, or if two major and two minor features are present.⁴ In our patient, the diagnosis of Beçhet's disease is supported by the coexistence of aphthous ulceration, uveitis, retinal vasculitis, folliculitis, brain stem involvement and the histopathological findings.

The association of neurological symptoms with Beçhet's disease was first reported by Knapp in 1941.⁵ Later, Berlin reported the first autopsy case of Beçhet's disease with involvement of the central nervous system.⁶ Approximately 25% of patients with Beçhet's disease have neurological manifestations, although these antedate the more diagnostic criteria of aphthous stomatitis, genital ulceration and uveitis in only 5% of cases.⁷ Neuropathological criteria for neuro-Beçhet's disease have not yet been fully established. An early classification divided the neurological manifestations of Beçhet's disease into three groups of brain stem syndrome, organic confusional state and meningomyelitic illness. Since then, many other neurological manifestations have been reported, including cranial nerve palsies, meningoencephalitis, hemiparesis, pseudobulbar palsy, epilepsy,

spinal cord involvement with Brown-Séquad syndrome and benign intracranial hypertension.^{8, 9} Peripheral nervous system involvement in Beçhet's disease is rare: we could find reports of only eleven cases, of which three had mononeuritis multiplex.^{10, 11, 12}

The clinical evidence of brain stem involvement in the final stages of our patient's illness is in keeping with previous pathological observations, which have shown this to be the commonest site for neurological involvement in Beçhet's disease. Computerised tomography of patients with neuro-Beçhet's disease has no pathognomonic features. Our patient's first computerised tomographic scan showed no abnormality, the second showed multiple low attenuation areas in the brain-stem and periventricular areas compatible with the post mortem finding of infarction. It has been suggested that magnetic resonance imaging may be more sensitive than CT scanning for detecting brain stem involvement in patients with neuro-Beçhet's syndrome.^{13, 14} Therapeutic options in severe Beçhet's disease include steroid and azathioprine therapy, chlorambucil, cyclophosphamide or acyclovir therapy.¹⁵ Assessment of treatment is difficult due to the rarity of the disease and its unpredictable course. The absence of response to prednisolone therapy is not unusual: in one series of 75 patients with Beçhet's disease with neurological involvement, steroids were ineffective in 50%.¹⁶ Clinical remission and disappearance of magnetic resonance imaging changes have been observed following high dose steroid therapy, albeit in small numbers of patients.^{14, 17} Whilst the effect of prednisolone therapy on the neurological manifestations of Beçhet's disease is unpredictable, the treatment of retinal vasculitis has been clarified: urgent therapy with local and systemic steroids is indicated to limit visual loss.¹

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